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| 10/647,361 | 08/25/2003 | Mark L. Weiss | KSURF-08401 | 2222 |

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| EXAMINER | |
|---|---|
| TON, THAIAN N | |

| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/647,361 | WEISS ET AL. | |
| | Examiner | Art Unit | |
| | Thaian N. Ton | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3,12-14,16-21,32-35 and 41-43* is/are pending in the application.

4a) Of the above claim(s) *14,32 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,12,13,16-21,34,35 and 41-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/11/09 has been entered.

Applicants' Amendment and Response, filed 5/11/09 has been entered. Claims 1, 3, 12-14, 16-21, 32-35, 41-43 are pending; claims 1, 3, 12, 34, 35, 41-43 are amended; claims 14, 32 and 33 are withdrawn; claims 1, 3, 12, 13, 16-21, 34-35, 41-43 are under current examination.

### *Election/Restrictions*

Claims 14, 32 and 33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/14/06.

Applicant's election without traverse of Group I (claims 1-3, 12, 13, 16-22, 34, 35 and 41-43) in the reply filed on 8/14/06 is acknowledged.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 12, 13, 16-21, 34-35, 41-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

1. A method for obtaining a population of cells from an umbilical cord matrix comprising:

a) enzymatically dispersing umbilical cord matrix to provide enzymatically dispersed umbilical cord matrix cells;

b) culturing the enzymatically dispersed umbilical cord matrix cells in the presence of epidermal growth factor (EGF) and platelet derived growth factor (PDGF) to proliferate the umbilical cord matrix cells;

c) culturing the enzymatically dispersed umbilical cord matrix cells on a substrate surface and removing non-adherent cells;

d) *culturing adherent cells* from c) to select for a population of umbilical cord matrix cells that *comprise cells* that are negative for CD34 and CD45, positive for telomerase activity, can be expanded in vitro, and maintained in culture through repeated passages.

2. A population of umbilical cord *matrix* cells isolated by a) enzymatically dispersing umbilical cord matrix to provide enzymatically dispersed umbilical cord matrix cells;

b) culturing the enzymatically dispersed umbilical cord matrix cells in the presence of epidermal growth factor (EGF) and platelet derived growth factor (PDGF) to proliferate the umbilical cord matrix cells;

c) culturing the enzymatically dispersed umbilical cord matrix cells on a substrate surface and removing non-adherent cells;

d) *culturing adherent cells* from c) to select for a population of umbilical cord matrix cells that *comprise cells* that are negative for CD34 and CD45, positive

for telomerase activity, can be expanded in vitro, and maintained in culture through repeated passages.

3. Methods of banking the population of cells recited in #2.

4.. Umbilical cord matrix cell cultures comprising a population of umbilical cord matrix cells as recited in #2 and a feeder cell population.

The specification does not reasonably provide enablement for 1) passaging the enzymatically dispersed umbilical cord matrix cells to remove non-adherent cells absent culturing the cells on a substrate surface and 2) a population of cells, wherein the entire population of cells is characterized by being negative for CD34, CD45, positive for telomerase activity, can be expanded in vitro and maintained in culture through repeated passages. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Applicants' arguments are found to be persuasive with regard to the following aspects of the prior rejection: the claims have now been amended to recite a method of obtaining a population of cells from an umbilical cord matrix, and therefore no longer recite enriching for umbilical cord matrix stem cells. The working examples and the specification support producing a heterogeneous population of cells from umbilical cord matrix, as instantly claimed, therefore, the

prior rejection of record, regarding UCMS cells, and the characterization thereof, is withdrawn.

The claims are not found to be enabling for the following reasons:

1. Passaging of Cells. The claims recite that the enzymatically dispersed umbilical cord matrix cells are "passaged to remove non-adherent cells, thus selecting a population of cells that are characterized by being negative for CD34, CD45, positive for telomerase activity, can be expanded in vitro and maintained in culture through repeated passages. However, the specification does not enable this method step because the specification teaches culturing cells to a substrate surface and removing of non-adherent matter (pp. 8-9, bridging ¶). Thus, for the instant method to be enabled, a substrate for the desired cells to adhere to must be present. Additionally, the step of removing the non-adherent cells and selection of the UCM cells is not produced by passaging of the cells, but is an active removal step. That is, the claims as written suggest that passaging passively results in removal of the non-adherent cells, whereas the specification makes clear that removal of the non-adherent cells is in context of allowing UCM cells to adhere to a substrate, and then removal of the non-adherent cells. The scope of enablement reflects these enabled method steps.

2) Characterization of the population of cells. The claims are written are not enabled because the recite that the population of cells "is characterized by being negative for CD34, CD45, positive for telomerase activity, can be expanded in vitro and maintained in culture through repeated passages". The claimed methods, working examples in the specification, as well as Applicants' remarks, teach that the method steps result in a heterogeneous population of cells that are isolated from umbilical cord matrix. Thus, as written, the claims recite that all of the cells in the population have the specific characteristics of being negative for CD34, CD45, positive for telomerase activity, can be expanded in vitro and maintained in culture through repeated passages. As noted in the prior Office actions, it is unclear from

the specification if a single cell type or multiple cells possess these characteristics. The specification fails to provide guidance for a homogenous cell population that has the recited characteristics; therefore, the enabled scope of the claimed invention has been determined that the cell population comprises cells that possess the claimed characteristics.

Accordingly, in view of the teachings and guidance provided by the specification, the claimed invention is found to be only enabling for culturing the enzymatically dispersed umbilical cord matrix cells on a substrate surface and removing non-adherent cells; *culturing adherent cells* to select for a population of umbilical cord matrix cells that *comprise cells* that are negative for CD34 and CD45, positive for telomerase activity, can be expanded in vitro, and maintained in culture through repeated passages. One of ordinary skill in the art would have had to practice undue experimentation to passage UCM cells to remove non-adherent cells, or produce a homogeneous population of UCM cells with the claimed characteristics.

### *Written Description*

The prior rejection of claims 1, 3, 12, 13, 16-21, 34-35, 41-43 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicants' amendment to the claims which no longer require enrichment of the cell population for UCMS cells.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 16-21, 34, 35, 41 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13, 16-21 recite the limitation "the umbilical cord matrix stem cell". The claims refer to claim 12, which is directed to a population of umbilical cord matrix cells (not stem cells). Therefore, there is insufficient antecedent basis for this limitation in the claim.

Claim 16 recites the limitation "the fraction of cells enriched for UCMS cells" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim 17 is unclear. The claim recites that the UCMS cells are from "any amniotic species". It is unclear what non-amniotic species of animal are encompassed by the claims which would have umbilical cords. Appropriate correct is requested.

Claim 34 is unclear. The claim recites that the cells "maintain a karyotype in which all the chromosomes of the human are present..." (see last 3 lines of the claim). The metes and bounds of the claims are unclear because claim 34 does not relate to a population of human cells; thus, it is unclear what "all the chromosomes of the human" refer to, and what it means to exclude. Claim 35 depends from claim 34.

Claim 35 recites the limitations "the stem cells" in line 1 of the claim and "comprising human UCMS cells" in line 2. There is insufficient antecedent basis for these limitations in the claim.

Claim 41 is unclear. The claim recites that the population of cells is "enriched for umbilical cord cells". The cells are isolated from umbilical cord matrix, therefore, it is unclear how the cells are "enriched in umbilical cord matrix cells" because these cells are not a particular cell type. Given that the starting material is umbilical cord matrix cells, the steps are unclear with regard to how

they result in an enriched population of the same cells. Claim 42 depends from claim 41.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 34, 35 stand rejected under 35 U.S.C. 102(b) as being anticipated by Purchio *et al.*(**US Pat. No. 5,919,702**, July 6, 1999).

*Applicants' Arguments*. Applicants argue that Purchio do not anticipate the claimed invention because they do not teach the use of growth factors, EGF and PDGF, in the media. Additionally, Applicants argue that the claimed process is novel over Purchio and the cell population produced by the claimed process is different than the cell population produced by Purchio as established in the Mitchell Declaration.

*Response to Arguments*. These arguments have been considered but are not persuasive. In particular, claims 3, 34 and 35 relate to a population of cells; therefore, Applicants' arguments regarding EGF and PDGF in the media are not relevant to the claimed invention. Additionally, Applicants have not provided any guidance or evidence to show that the presence of EGF and PDGF in the media results in a patentable distinction between the instantly claimed cells and that taught by Purchio.

With regard to the Mitchell Declaration, the Examiner has previously responded to Applicants' arguments with regard to the cell populations taught by the instant methods and the cells taught by Purchio. In short, the Examiner

reiterates that the arguments by Applicants, as well as the Mitchell Declaration appear to argue that the method of isolation of the UCM cells of the instant invention provides a patentable distinction between the claimed population of cells, and that which is produced by Purchio. Preliminarily, certain embodiments are directed to "enriched" populations of UCM cells, however, as discussed above, this term does not provide patentable weight. Broadly interpreted, the claims encompass any population of cells that has any amount of UCM cells. Given that the claims do not require any degree of enrichment, and in view of the specification's teaching that the stripping of umbilical vessels would still result in the production of UCMS cells, the Examiner maintains that there would a reasonable expectation that the methods of Purchio, who discuss isolating, collecting and culturing Wharton's jelly would contain some UCMS cells.

The rejection is based upon the claims, which broadly encompass any population of cells that contain UCM cells. Purchio teaches the isolation and culture of Wharton's jelly, which also contains UCM cells. Therefore, given that Purchio teaches cells that are isolated from the same source, and produced by methods that are taught by the specification, the Wharton's jelly culture that is taught by Purchio anticipates the instant claims.

***Rejection***

Purchio teach cultures of Wharton's jelly (see col. 10-11, #5.1) that can be cultured and expanded. Accordingly, because Purchio teach a culture of cells from the same source as the instantly claimed cell compositions, Purchio's culture would inherently contain the cell compositions and cultures as instantly claimed. Therefore, any properties claimed for the cells would also be necessarily present. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant

discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Claims 3, 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (**Science**, 282: 1145-1147, November 6, 1998) as evidenced by Kaufman *et al.* (**PNAS**, 98(19): 10716-10721, 2001) and evidenced by Hoffman *et al.* (**Nature Biotech.**, 23(6): 699-708, 2005).

The claims are product-by-process claims (see above). The only structural limitations of the claims are that they are characterized by being negative for CD34 and CD56, positive for telomerase activity, can be expanded in vitro and maintained in culture for repeated passages (claim 3); and further can proliferate in an *in vitro* culture for over one year, maintain a karyotype in which all the chromosomes are present and not noticeably altered through prolong culture and maintain the potential to differentiate. Thus, cells that fulfill these limitations are not patentably distinguishable from the instant claims.

Thomson teach the derivation of a human ES cell line, H1. They teach that the H1 cell line has a normal XX karyotype. See p. 1145, col. 2. Thomson teach that the ES cell line expresses telomerase (p. 1145, col. 3, 1st full ¶). Kaufman is

provided as evidence that the H1 ES cell line does not express CD34 or CD45 (p. 10718, col. 1, 1st ¶). Hoffman is provided as evidence that the H1 ES cell line can be cultured through repeated passages and maintain a normal karyotype (p. 702, col. 1, Cytogenetic Analysis). Hoffman further shows that H1 retains the potential to differentiate (see Table 2).

Accordingly, Thomson anticipate the claims.

## *Conclusion*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (571)272-0736. The examiner can normally be reached on 9-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thaian N. Ton/
Primary Examiner, Art Unit 1632